

Appl. No. 10/717,197  
Amdt. Dated  
Reply to Office action of March 3, 2004

**Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1-22 cancelled.

Please add the following new claims:--

23. (New) A combined preparation for simultaneous, separate or sequential use as an ultrasound contrast agent, said preparation comprising:

- i) an injectable aqueous gas dispersion; and
- ii) a separately administrable substance or substances capable of destabilising

said dispersed gas so as at least transiently to increase the size thereof.

24. (New) A combined preparation as claimed in claim 23 wherein the dispersed gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulphur fluoride, selenium hexafluoride, an optionally halogenated silane, an optionally halogenated low molecular weight hydrocarbon, a ketone, an ester or a mixture of any of the foregoing.

25. (New) A combined preparation as claimed in claim 24 wherein the dispersed gas comprises sulphur hexafluoride or a perfluorocarbon.

26. (New) A combined preparation as claimed in claim 25 wherein said perfluorocarbon is perfluoropropane, perfluorobutane or perfluoropentane.

27. (New) A combined preparation as claimed in claim 23 wherein the dispersed gas is

stabilised by an initially coalescence-resisting surface membrane, a filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.

28. (New) A combined preparation as claimed in claim 27 wherein said surfactant

comprises at least one phospholipid.

29. (New) A combined preparation as claimed in claim 28 wherein at least 75% of said

surfactant comprises phospholipid molecules individually bearing net overall charge.

30. (New) A combined preparation as claimed in claim 29 wherein said charged

phospholipid molecules are selected from phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, phosphatidic acid and cardiolipin molecules.

31. (New) A combined preparation as claimed in claim 23 wherein said administrable

substance further comprises one or more destabilising substances which induce growth of the dispersed gas by flocculation, aggregation, agglomeration, coalescence, fusion or Ostwald ripening.

32. (New) A combined preparation as claimed in claim 31 comprising one or more

destabilising substances selected from the group consisting of inorganic salts, aliphatic alcohols, aliphatic aldehydes, aliphatic ketones, aliphatic esters, aliphatic

ethers, aliphatic amides, aliphatic nitriles, carbohydrates, polyethers, polysaccharides, polyaminoacids, polyvinylpyrrolidone, fatty alcohols, fatty acids, fatty amines, surfactants, steroids, acids, bases and hydrotropes.

33. (New) A combined preparation as claimed in claim 32 comprising one or more destabilising substances selected from the group consisting of calcium chloride, magnesium chloride, ethanol, isopropanol, ethylene glycol, propylene glycol, glycerol, sorbitol, acetaldehyde, acetone, methyl formate, methyl acetate, propyl formate, ethyl acetate, ethyl methyl ether, methyl propyl ether, di-isopropyl ether, N,N-dimethylformamide, N,N-dimethylacetamide, acetonitrile, glucose, sucrose, polyethylene glycol, polypropylene glycol, polyoxyethylene-polyoxypropylene block copolymers, dextran, starches, polylysine, gelatin, cholesterol, and surface active alkyl carboxylates, alkyl sulphonates, alkyl sulphates, dialkyl sulphosuccinates, alkyl pyridinium salts, alkylammonium salts, alkyl polyethylene glycol ethers, alkyl polyethylene glycol esters and sorbitol fatty acid esters.

34. (New) A combined preparation as claimed in claim 23 which further includes a vasodilator drug.

35. (New) A combined preparation as claimed in claim 34 wherein said vasodilator drug is adenosine.

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36. (New) A combined preparation as claimed in claim 23 which further includes a therapeutic drug.

37. (New) A combined preparation as claimed in claim 23 which further includes contrast-enhancing moieties for an imaging modality other than ultrasound.

38. (New) A method of generating enhanced images of a human or non-human animal subject which comprises the steps of:

- i) injecting a physiologically acceptable aqueous medium having gas dispersed therein into the vascular system of said subject;
- ii) before, during or after injection of said aqueous medium administering to said subject a substance capable of destabilising said dispersed gas so as at least transiently to increase the size thereof; and
- iii) generating an ultrasound image if at least a part of said subject.

39. (New) A method as claimed in claim 38 wherein destabilising substance is administered subcutaneously, intramuscularly, intravenously or by inhalation.

40. (New) A method as claimed in claim 38 wherein a vasodilator drug is co-administered to the subject.

41. (New) A method as claimed in claim 40 wherein said vasodilator drug is adenosine.

42. (New) A method of therapeutically treating a human or non-human animal subject which

comprises the steps of:

i) injecting a physiologically acceptable aqueous gas dispersion into the

vascular system of said subject;

ii) before, during or after injection of said aqueous gas dispersion

administering to said subject a substance capable of destabilising said dispersed gas;

iii) growth and retention of said dispersed gas within the tissue

microvasculature of the site of interest of said subject and thereby killing cells or

blocking the blood flow to the site.

43. (New) A method of therapeutically treating a human or non-human animal subject which

comprises the steps of:

i) injecting a physiologically acceptable aqueous gas dispersion into the

vascular system of said subject;

ii) before, during or after injection of said aqueous gas dispersion administering to

said subject a substance capable of destabilising said dispersed gas;

iii) growth and retention of said dispersed gas within the tissue

microvasculature of the site of interest;

iv) applying ultrasonic irradiation to said site of interest and thereby enhance

absorption of ultrasonic energy in hyperthermic therapy.--